=> d his

(FILE 'HOME' ENTERED AT 11:52:08 ON 06 JUN 2003)

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 11:52:23 ON 06 JUN 2003

SEA COX-2	
499	FILE ADISCTI
67	FILE ADISINSIGHT
187	FILE ADISNEWS
34	FILE AGRICOLA
7	FILE ANABSTR
9	FILE AQUASCI
56	FILE BIOBUSINESS
8	FILE BIOCOMMERCE
5794	FILE BIOSIS
39	FILE BIOTECHABS
39	FILE BIOTECHDS
1401	FILE BIOTECHNO
235	FILE CABA
1476	FILE CANCERLIT
4917	FILE CAPLUS
7	FILE CEABA-VTB
6	FILE CEN
231	FILE CIN
91	FILE CONFSCI
2	FILE CROPU
2167	FILE DDFU
502	FILE DGENE
1	FILE DRUGLAUNCH
1	FILE DRUGMONOG2
176	FILE DRUGNL
2484	FILE DRUGU
55	FILE DRUGUPDATES
194	FILE EMBAL
4288	FILE EMBASE
2916	FILE ESBIOBASE
352	FILE FEDRIP
1	FILE FOMAD
17	FILE FROSTI
12	FILE FSTA
56	FILE GENBANK
9	FILE HEALSAFE
375	FILE IFIPAT
405	FILE JICST-EPLUS
1	FILE KOSMET
685	FILE LIFESCI
39	FILE MEDICONF
4411	FILE MEDLINE
1	FILE NIOSHTIC
22	FILE NTIS
6	FILE NUTRACEUT
2301	FILE PASCAL
76	FILE PHAR
281	FILE PHARMAML
7	FILE PHIC
515	FILE PHIN
1042	FILE PROMT
5269	FILE SCISEARCH
19	FILE SYNTHLINE

```
             4301   FILE TOXCENTER
             1213   FILE USPATFULL
               91   FILE USPAT2
               33   FILE VETU
              505   FILE WPIDS
              505   FILE WPINDEX
L1               QUE COX-2
                 ---------

     FILE 'BIOSIS, SCISEARCH, CAPLUS, MEDLINE, TOXCENTER, EMBASE, ESBIOBASE,
     DRUGU, PASCAL, CANCERLIT' ENTERED AT 11:54:20 ON 06 JUN 2003
L2             9 S L1 AND GALPHA12
L3             3 DUP REM L2 (6 DUPLICATES REMOVED)
L4             6 S L1 AND GALPHA
L5             3 DUP REM L4 (3 DUPLICATES REMOVED)

=> log Y
```

L3 3 DUP REM L2 (6 DUPLICATES REMOVED)

=> d l3 ibib ab 1-3

L3 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2003:103504 BIOSIS
DOCUMENT NUMBER: PREV200300103504
TITLE: Galphaq signaling is required for Rho-dependent transcriptional activation of the cyclooxygenase-2 promoter in fibroblasts.
AUTHOR(S): Slice, Lee W. (1); Han, Sang-kyou; Simon, Melvin I.
CORPORATE SOURCE: (1) University of California, 900 Veteran Avenue, Los Angeles, CA, 90095-1786, USA: lslice@mednet.ucla.edu USA
SOURCE: Journal of Cellular Physiology, (February 2003, 2003) Vol. 194, No. 2, pp. 127-138. print.
ISSN: 0021-9541.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Previously, we demonstrated that the gastrin releasing peptide (GRP) induces cyclooxygenase-2 (**COX-2**) expression through a Rho-dependent, protein kinase C (PKC)-independent signaling pathway in fibroblasts (Slice et al., 1999, J Biol Chem 274:27562-27566). However, the specific role of heterotrimeric guanine nucleotide binding regulatory proteins (G-proteins) that are coupled to the GRP receptor in Rho-dependent **COX-2** expression has not been elucidated. In this report, we utilize embryonic fibroblasts from transgenic mice containing double gene knock-outs (DKO) for Galphaq/11 and **Galpha12**/13 to demonstrate that **COX-2** promoter activation by GRP requires Galphaq. Furthermore, we show that GRP-dependent **COX-2** gene expression, as assessed by a **COX-2** reporter luciferase assay, was induced in cells lacking **Galpha12**/13 but was blocked in cells that did not express Galphaq/11. GRP-dependent **COX-2** promoter induction in Galphaq/11 deficient cells was rescued by expression of wild type Galphaq but blocked by inhibition of calcium signaling in calcium-free media or in cells treated with 2-aminoethoxydiphenylborate (2-APB). Co-stimulation of transfected Galphaq/11 deficient cells with GRP and thapsigargin (TG) induced the **COX-2** promoter. Activation of endogenous Rho by expression of Onco-lbc or expression of Rho A Q63L resulted in **COX-2** promoter activation in Galphaq/11 deficient cells. Inhibition of Rho by Clostridium botulinum C3 toxin blocked **COX-2** promoter induction. Expression of Galphaq Q209L in the well-characterized fibroblast cell line, NIH3T3, induced the **COX-2** promoter which was blocked by expression of C3 toxin. These results demonstrate that calcium signaling mediated by Galphaq and Rho play critical roles in GRP-dependent **COX-2** expression in fibroblasts.

L3 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
ACCESSION NUMBER: 2001:344364 BIOSIS
DOCUMENT NUMBER: PREV200100344364
TITLE: Activation of cellular invasion by trefoil peptides and src is mediated by cyclooxygenase- and thromboxane A2 receptor-dependent signaling pathways.
AUTHOR(S): Rodrigues, Sylvie; Nguyen, Quang-De; Faivre, Sandrine; Bruyneel, Erik; Thim, Lars; Westley, Bruce; May, Felicity; Flatau, Gilles; Mareel, Marc; Gespach, Christian (1); Emami, Shahin
CORPORATE SOURCE: (1) INSERM Unit U482, Hopital Saint-Antoine, 75571, Paris Cedex 12: gespach@st-antoine.inserm.fr France
SOURCE: FASEB Journal, (July, 2001) Vol. 15, No. 9, pp. 1517-1528. print.
ISSN: 0892-6638.
DOCUMENT TYPE: Article

LANGUAGE: English
SUMMARY LANGUAGE: English
AB We have investigated the possible functional relationships between cellular invasion pathways induced by trefoil factors (TFFs), src, and the cyclooxygenases COX-1 and **COX-2**. Pharmacological inhibitors of the Rho small GTPase (C3 exoenzyme), phospholipase C (U-73122), cyclooxygenases (SC-560, NS-398), and the thromboxane A2 receptor (TXA2-R) antagonist SQ-295 completely abolished invasion induced by intestinal trefoil factor, pS2, and src in kidney and colonic epithelial cells MDCKts.src and PCmsrc. In contrast, invasion was induced by the TXA2-R mimetic U-46619, constitutively activated forms of the heterotrimeric G-proteins Galphaq (AGalphaq), **Galpha12**, Galpha13 (AGalpha12/13), which are signaling elements downstream of TXA2-R. Ectopic overexpression of pS2 cDNA and protein in MDCKts.src-pS2 cells and human colorectal cancer cells HCT8/S11-pS2 initiate distinct invasion signals that are Rho independent and COX and TXA2-R dependent. We detected a marked induction of **COX-2** protein and accumulation of the stable PGH2/TXA2 metabolite TXB2 in the conditioned medium from cells transformed by src. This led to activation of the TXA2-R-dependent invasion pathway, which is monitored via a Rho- and **Galpha12** /Galpha13-independent mechanism using the Galphaq/PKC signaling cascade. These findings identify a new intracrine/paracrine loop that can be monitored by TFFs and src in inflammatory diseases and progression of colorectal cancers.

L3 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
ACCESSION NUMBER: 2000:59882 BIOSIS
DOCUMENT NUMBER: PREV200000059882
TITLE: Oncogenic mutant of **Galpha12** stimulates cell proliferation through cycloxygenase-2 signaling pathway.
AUTHOR(S): Dermott, Jonathan M.; Reddy, M.V. Ramana; Onesime, Djamila; Reddy, E. Premkumar; Dhanasekaran, N. (1)
CORPORATE SOURCE: (1) Fels Institute for Cancer Research and Molecular Biology, Temple University School of Medicine, Philadelphia, PA USA
SOURCE: Oncogene, (Dec. 2, 1999) Vol. 18, No. 51, pp. 7185-7189. ISSN: 0950-9232.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Expression of the GTPase-deficient, activated mutant alpha-subunit of the heterotrimeric G protein G12 (Galpha12QL) leads to the neoplastic transformation of fibroblast cell lines. The mitogenic pathway regulated by Galpha12QL includes an extensive signaling network involving several small GTPases and various kinases. In addition, Galpha12QL has been shown to potentiate the serum-induced phospholipase-A2 activity in NIH3T3 cells. In the present study, we demonstrate that cycloxygenase-2 (**COX-2**) pathway is involved in the mitogenic pathway activated by Galpha12QL. Expression of Galpha12QL and not Galpha13QL, stimulates the serum-induced release of arachidonic acid in NIH3T3 cells. Furthermore, expression of Galpha12QL or the stimulation of wild-type **Galpha12** induces the expression of **COX-2**. Our results also indicate that the **COX-2** inhibitor acutely disrupts the DNA-synthesis stimulated by Galpha12QL in NIH3T3 cells. These studies, for the first time, identify the crucial role of **COX-2** in **Galpha12**-mediated regulation of cell proliferation and suggest a role for prostaglandin-derived autocrine loop in **Galpha12** -mediated signaling pathways.

WEST

Help | Logout | Interrupt

Main Menu | Search Form | Posting Counts | Show S Numbers | Edit S Numbers | Preferences | Cases

Search Results -

Terms	Documents
L1 same (G protein)	12

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L6

Refine Search | Recall Text | Clear

Search History

DATE: Saturday, June 07, 2003 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
L6	L1 same (G protein)	12	L6
L5	L1 same (Galpha12)	0	L5
L4	L1 and Galpha12	0	L4
L3	L2 same (GTPase mutant)	0	L3
L2	L1 same Galpha12	0	L2
L1	COX-2	1698	L1

END OF SEARCH HISTORY

WEST

Help | Logout | Interrupt

Main Menu | Search Form | Posting Counts | Show S Numbers | Edit S Numbers | Preferences | Cases

Search Results -

Terms	Documents
L1 same (G protein)	12

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L6

Refine Search

Recall Text | Clear

Search History

DATE: Saturday, June 07, 2003 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
L6	L1 same (G protein)	12	L6
L5	L1 same (Galpha12)	0	L5
L4	L1 and Galpha12	0	L4
L3	L2 same (GTPase mutant)	0	L3
L2	L1 same Galpha12	0	L2
L1	COX-2	1698	L1

END OF SEARCH HISTORY

1: Jpn J Cancer Res. 1997 Nov;88(11):1044-51. Related Articles, Links

Entrez PubMed

PubMed Services

Related Resources

Inhibitory effect of NS-398, a selective cyclooxygenase-2 inhibitor, on azoxymethane-induced aberrant crypt foci in colon carcinogenesis of F344 rats.

Yoshimi N, Kawabata K, Hara A, Matsunaga K, Yamada Y, Mori H.

Department of Pathology, Gifu University School of Medicine.

Prostaglandin E2, which is produced by cyclooxygenase (COX) during arachidonic acid metabolism, is considered to be related to colon carcinogenesis. Therefore, the effect of NS-398 (N-(2-cyclohexyloxy-4-nitrophenyl)methanesulfonamide), a COX-2 inhibitor, was examined in azoxymethane (AOM)-induced colon carcinogenesis in rats in this study. In the first experiment, groups 1-3 were treated with AOM (15 mg/kg, s.c.) 3 times at intervals of a week from 5 weeks of age. Groups 2 and 3 were respectively given 1 mg/kg and 10 mg/kg of NS-398 in 5% gum arabic aqueous solution 3 times per week by oral gavage during the experiment. Six weeks after the first exposure to AOM, aberrant crypt foci (ACF) were counted in the colonic mucosa of all rats. The mean occurrence of ACF per length in rats given 1 mg/kg b.w. or 10 mg/kg b.w. of NS-398 was reduced to 65.7% or 52.8%, respectively, of that in rats treated with only AOM. Levels of COX-2 mRNA expression in groups treated with AOM, regardless of NS-398, were slightly higher than that in the group treated with NS-398 alone as judged from reverse transcription-polymerase chain reaction analysis. In the second experiment, the effect of NS-398 at different times, i.e., during initiation and post-initiation, was examined. Treatment with NS-398 in both phases significantly inhibited the appearance of ACF. The results imply that NS-398 might have a chemopreventive potential.

PMID: 9439679 [PubMed - indexed for MEDLINE]

1: Jpn J Cancer Res. 1997 Dec;88(12):1117-20. Related Articles, Links

Entrez PubMed

PubMed Services

Related Resources

Suppression of intestinal polyp development by nimesulide, a selective cyclooxygenase-2 inhibitor, in Min mice.

Nakatsugi S, Fukutake M, Takahashi M, Fukuda K, Isoi T, Taniguchi Y, Sugimura T, Wakabayashi K.

Cancer Prevention Division, National Cancer Center Research Institute, Tokyo.

Nonsteroidal anti-inflammatory drugs (NSAIDs) suppress colon carcinogenesis in man and experimental animals. However, conventional NSAIDs inhibit both cyclooxygenase (COX) isoforms, COX-1 and COX-2, and cause gastrointestinal side-effects. Nimesulide, a selective inhibitor of COX-2, is much less ulcerogenic. We, therefore, examined its influence on the development of intestinal polyps in Min mice. Female Min mice at 4 weeks old were given 400 ppm nimesulide in their diet for 11 weeks. This treatment resulted in a significant reduction of the numbers of both small and large intestinal polyps, the total being 52% of that in untreated control Min mice. The size of the polyps in the nimesulide-treated group was also significantly decreased. The results suggest that nimesulide is a good candidate as a chemopreventive agent for human colon cancer with low toxicity.

PMID: 9473726 [PubMed - indexed for MEDLINE]

Display Abstract Show: 20 Sort Send to Text

1: Inflamm Res. 1997 Dec;46(12):496-502. Related Articles, Links

Entrez PubMed

Inflammation Research

Selective inhibition of cyclooxygenase-2 by NS-398 in endotoxin shock rats in vivo.

Futaki N, Takahashi S, Kitagawa T, Yamakawa Y, Tanaka M, Higuchi S.

Pharmaceutical Research Laboratories, Taisho Pharmaceutical Co. Ltd., Saitama, Japan.

PubMed Services

OBJECTIVE AND DESIGN: The role of cyclooxygenase (COX)-2 was examined using a rat endotoxin shock model and the potency and selectivity of NS-398, a COX-2 selective inhibitor in vitro, for COX-2 activity was examined in vivo. MATERIAL: Male Wistar rats (weighing 140-180 g) were used. METHODS: Lipopolysaccharide (LPS, 1 mg/kg, i.v.) was administered to rats (LPS-treated rats) and expression of COX-1 mRNA and COX-2 mRNA in the aorta and peripheral blood leukocytes was examined by RT-PCR. COX activity was assessed by measuring the plasma 6-keto prostaglandin (PG) F1 alpha, PGE2 and thromboxane (TX)B2 30s after administration of arachidonic acid (AA, 3 mg/kg, i.v.), NS-398 (0.3-100 mg/kg, p.o.) or indomethacin (0.3-3 mg/kg, p.o.) was administered 1 h before the AA injection. RESULTS: COX-2 mRNA was detectable in the aorta and peripheral blood leukocytes at least from 3 to 9 h after the LPS injection but not in non-LPS-treated rats. Plasma 6-keto PGF1 alpha, PGE2 and TXB2 levels after AA injection into LPS-treated rats were significantly enhanced compared to findings in non-LPS-treated rats. NS-398 showed significant inhibition of the increase in PGs in LPS-treated rats, the ED50 values being 0.35 mg/kg for 6-keto PGF1 alpha, 1.5 mg/kg for PGE2 and < 0.3 mg/kg for TXB2. NS-398 even at 100 mg/kg did not significantly suppress the increased PGs levels in non-LPS-treated rats. In contrast, indomethacin significantly inhibited plasma PGs levels after AA injection into LPS-treated rats and non-LPS-treated rats. The ED50 values in LPS-treated rats, determined by 6-keto PGF1 alpha, PGE2 and TXB2 production, were 1.0, 1.3 and 2.3 mg/kg and those in non-LPS-treated rats were 0.42, 0.24 and 0.93 mg/kg, respectively. CONCLUSIONS: In a rat endotoxin shock model, expression of COX-2 plays a role in an increase in COX activity. NS-398 showed preferential inhibitory effects on COX-2 activity in vivo. This approach is useful to directly analyze the inhibitory activity of NSAIDs for COX-1 and COX-2 in vivo.

Related Resources

PMID: 9459080 [PubMed - indexed for MEDLINE]

1: Inflamm Res. 1997 Nov;46(11):437-46. Related Articles, Links

Entrez PubMed

In vitro and in vivo pharmacological evidence of selective cyclooxygenase-2 inhibition by nimesulide: an overview.

Famaey JP.

Therabel Research S.A., Brussels, Belgium.

PubMed Services

Related Resources

Most available nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit both the constitutive cyclooxygenase-1 (COX-1) and the inducible cyclooxygenase-2 (COX-2), resulting in inhibition of prostaglandin (PG) and thromboxane (TX) biosynthesis. The inhibition of COX-2 might be the cause of the favourable anti-inflammatory, analgesic and antipyretic effects of NSAIDs, whereas that of COX-1 might result in unwanted gastrointestinal, renal and possibly other side-effects. Nimesulide is a sulfonanilide compound with anti-inflammatory properties. Its pharmacological profile (better inhibition of PG synthesis in inflammatory areas than in gastric mucosa), suggested that it might be a selective inhibitor of COX-2. In several in vitro assays using either purified COX-2 and COX-1 preparations or cell preparations (both from animal and human origins) expressing COX-1 or COX-2, ten out of eleven different groups have demonstrated that nimesulide selectively inhibits COX-2. The COX-2/ COX-1 inhibitory ratio varies, according to the assay preparation, from about 0.76 to 0.0004 i.e. a 1.3 to 2,512-fold higher selectivity for COX-2 than for COX-1. Moreover, an in vivo whole blood assay performed on healthy volunteers demonstrated a significant fall in COX-2 PGE2 production without any effect on COX-1 TXB2 production in subjects treated with nimesulide (100 mg b.i.d. for 2 weeks) versus no effect on COX-2 PGE2 and an almost total suppression of COX-1 TXB2 in subjects treated with aspirin (300 mg t.i.d. for 2 weeks). Nimesulide can thus be considered a relatively selective COX-2 inhibitor. At the recommended dosage of 100 mg b.i.d., it is as effective an analgesic and anti-inflammatory agent as classical NSAIDs, and a well-tolerated drug with few side-effects according to large-scale open studies and a global evaluation of a large number of controlled and non-controlled comparative trials.

Publication Types:
- Review
- Review, Tutorial

1: Annu Rev Biochem. 1986;55:69-102. Related Articles, Links

Arachidonic acid metabolism.

Needleman P, Turk J, Jakschik BA, Morrison AR, Lefkowith JB.

Publication Types:
- Review

PMID: 3017195 [PubMed - indexed for MEDLINE]

1: Prostaglandins Leukot Essent Fatty Acids. 1998 Jun;58(6):421-4.

Effects of lysine clonixinate on cyclooxygenase I and II in rat lung and stomach preparations.

Franchi AM, Di Girolamo G, de los Santos AR, Marti ML, Gimeno MA.

Centro de Estudios Farmacologicos y Botanicos (CEFYBO), Consejo Nacional de Investigaciones Cientificas y Tecnicas (CONICET), Buenos Aires, Argentina.

Lysine clonixinate (LC) is a drug of antiinflammatory antipyretic and analgesic activity that produces minor digestive side-effects. This fact induced us to think that LC is possibly a weak COX-1 inhibitor. In order to investigate our hypothesis we inhibited cyclooxygenase activity with LC or indomethacin (INDO) in rat lung and stomach obtained from rats treated with lipopolysacharide (LPS) and control rats. Rat lung preparations incubated with 14C-arachidonic acid synthesise mainly PGE2. LC at 2.5 and 4.1 x 10(-5) M does not modify the basal production of PGE2 (probably COX-1) but at 6.8 x 10(-5) M significantly inhibited PGE2 production (approximately 48.5% inhibition, P<0.001). On the other hand, INDO at 10(-6) inhibited the basal production of PGE2 by around 73%. In LPS-treated rats, the production of PGE2 was significantly higher than in the lungs of control rats, probably due to the induction of COX-2. The addition of LC at 2.7 and 4.1 x 10(-5) M recovered the control values of PGE2 inhibiting, probably only from COX-2 activity. LC at higher concentrations (6.8 x 10(-5) M) and INDO 10(-6) M inhibited PGE2 formed by COX-2 and also partly by COX-1 activity.

PMID: 10189073 [PubMed - indexed for MEDLINE]

1: J Physiol Pharmacol. 1998 Dec;49(4):501-13. Related Articles, Links

Entrez PubMed

PubMed Services

Related Resources

Cyclooxygenase-2 selective and nitric oxide-releasing nonsteroidal anti-inflammatory drugs and gastric mucosal responses.

Takeuchi K, Suzuki K, Yamamoto H, Araki H, Mizoguchi H, Ukawa H.

Department of Pharmacology & Experimental Therapeutics, Kyoto Pharmaceutical University, Yamashina, Japan. takeuchi@mb.kyoto-phu.ac.jp

Occurrence of gastrointestinal damage and delayed healing of pre-existing ulcer are commonly observed in association with clinical use of nonsteroidal antiinflammatory drugs (NSAIDs). We examined the effects of NS-398, the cyclooxygenase (COX)-2 selective inhibitor, and nitric oxide (NO)- releasing aspirin (NCX-4016) on gastric mucosal ulcerogenic and healing responses in experimental animals, in comparison with those of nonselective COX inhibitors such as indomethacin and aspirin. Indomethacin and aspirin given orally were ulcerogenic by themselves in rat stomachs, while either NS-398 or NCX-4016 was not ulcerogenic at the doses which exert the equipotent antiinflammatory action with indomethacin or aspirin. Among these NSAIDs, only NCX-4016 showed a dose-dependent protection against gastric lesions induced by HCl/ethanol in rats. On the other hand, the healing of gastric ulcers induced in mice by thermal-cauterization was significantly delayed by repeated administration of these NSAIDs for more than 7 days, except NCX-4016. Gastric mucosal prostaglandin contents were reduced by indomethacin, aspirin and NCX-4016 in both normal and ulcerated mucosa, while NS-398 significantly decreased prostaglandin generation only in the ulcerated mucosa. Oral administration of NCX-4016 in pylorus-ligated rats and mice increased the levels of NO metabolites in the gastric contents. In addition, both NS-398 and NCX-4016 showed an equipotent anti-inflammatory effect against carrageenan-induced paw edema in rats as compared with indomethacin and aspirin. These results suggest that both indomethacin and aspirin are ulcerogenic by themselves and impair the healing of pre-existing gastric ulcers as well. The former action is due to inhibition of COX-1, while the latter effect may be accounted for by inhibition of COX-2 and mimicked by NS-398, the COX-2 selective NSAID. NCX-4016, despite inhibiting both COX-1 and COX-2, protects the stomach against damage and preserves the healing response of gastric ulcers, probably because of the beneficial action of NO.

PMID: 10069692 [PubMed - indexed for MEDLINE]

1: Prostaglandins Other Lipid Mediat. 1998 Aug;56(5-6):277-90.

Lipopolysaccharide-induced expression of cyclooxygenase-2 in mouse macrophages is inhibited by chloromethylketones and a direct inhibitor of NF-kappa B translocation.

Abate A, Oberle S, Schroder H.

Department of Pharmacology and Toxicology, School of Pharmacy, Martin Luther University, Halle (Saale), Germany.

In macrophages, cyclooxygenase-2 (COX-2) is induced by cytokines, mitogens, or endotoxin. The present study investigates whether inhibitors of the nuclear transcription factor NF-kappa B affect lipopolysaccharide (LPS)-mediated expression of COX-2 mRNA, protein, and activity in the macrophage cell line J774.1A. The activation of COX-2 was assessed by measuring the accumulation of prostaglandin (PG) E2 by radioimmunoassay. Expression of COX-2 mRNA and protein was detected by Northern and Western blot analysis, respectively. In the absence of LPS, mouse macrophages did not express COX-2 and generated low amounts of prostaglandin (PG) E2. Treatment of J774.1A with LPS (0.1-30 micrograms/ml) caused expression of COX-2 protein and activity. Induction of COX-2 activity along with the induction of COX-2 mRNA and protein by LPS was attenuated by the serine protease inhibitors N-alpha-tosyl-L-phenylalanine chloromethyl ketone (TPCK) and N-alpha-tosyl-L-lysine chloromethyl ketone (TLCK). A cell permeable peptide and a direct inhibitor of NF-kappa B translocation, SN50, attenuated the accumulation of PGE2 in cell supernatant in a concentration-dependent manner. Our results show that induction of COX-2 by LPS in macrophages involves activation of NF-kappa B and point to a possible therapeutic use of protease inhibitors in inflammatory processes.

PMID: 9990673 [PubMed - indexed for MEDLINE]

1: Carcinogenesis. 1998 Dec;19(12):2195-9. Related Articles, Links

Entrez PubMed

PubMed Services

Related Resources

Meloxicam inhibits the growth of colorectal cancer cells.

Goldman AP, Williams CS, Sheng H, Lamps LW, Williams VP, Pairet M, Morrow JD, DuBois RN.

Department of Medicine, Vanderbilt University Medical Center, Nashville, TN 37232, USA.

Cyclooxygenase-2 has been reported to play an important role in colorectal carcinogenesis. The effects of meloxicam (a COX-2 inhibitor) on the growth of two colon cancer cell lines that express COX-2 (HCA-7 and Moser-S) and a COX-2 negative cell line (HCT-116) were evaluated. The growth rate of these cells was measured following treatment with meloxicam. HCA-7 and Moser-S colony size were significantly reduced following treatment with meloxicam; however, there was no significant change in HCT-116 colony size with treatment. In vivo studies were performed to evaluate the effect of meloxicam on the growth of HCA-7 cells when xenografted into nude mice. We observed a 51% reduction in tumor size after 4 weeks of treatment. Analysis of COX-1 and COX-2 protein levels in HCA-7 tumor lysates revealed a slight decrease in COX-2 expression levels in tumors taken from mice treated with meloxicam and no detectable COX-1 expression. Here we report that meloxicam significantly inhibited HCA-7 colony and tumor growth but had no effect on the growth of the COX-2 negative HCT-116 cells.

PMID: 9886578 [PubMed - indexed for MEDLINE]

NCBI PubMed National Library of Medicine NLM

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Books

Search PubMed for COX-2 inhibitor Preview Go

Clear

Limits Preview/Index **History** Clipboard Details

- Search History will be lost after one hour of inactivity.
- To combine searches use # before search number, e.g., #2 AND #6.
- Search numbers may not be continuous; all searches are represented.

Entrez PubMed

PubMed Services

Search	Most Recent Queries	Time	Result
#11	Search **COX-2 inhibitor** Field: **Title/Abstract,** Limits: **Publication Date from 1997 to 1997**	09:29:54	77
#10	Search **COX-2 inhibitor** Field: **Title/Abstract,** Limits: **Publication Date from 1990 to 1997**	09:29:37	136
#5	Search **COX-2 inhibitor** Field: **Title/Abstract,** Limits: **Publication Date from 1990 to 1998**	09:28:43	255
#3	Search **Dermott JM** Field: **Author,** Limits: **Publication Date from 1999 to 1999**	09:19:22	1
#1	Search **Laufer S** Field: **Author,** Limits: **Publication Date from 1999 to 1999**	09:18:15	1

Clear History

Related Resources

1: Oncogene. 1999 Dec 2;18(51):7185-9. Related Articles, Links

Oncogenic mutant of Galpha12 stimulates cell proliferation through cycloxygenase-2 signaling pathway.

Dermott JM, Reddy MR, Onesime D, Reddy EP, Dhanasekaran N.

Fels Institute for Cancer Research and Molecular Biology, Temple University School of Medicine, Philadelphia, Pennsylvania, PA 19140, USA.

Expression of the GTPase-deficient, activated mutant alpha-subunit of the heterotrimeric G protein G12 (Galpha12QL) leads to the neoplastic transformation of fibroblast cell lines. The mitogenic pathway regulated by Galpha12QL includes an extensive signaling network involving several small GTPases and various kinases. In addition, Galpha12QL has been shown to potentiate the serum-induced phospholipase-A2 activity in NIH3T3 cells. In the present study, we demonstrate that cycloxygenase-2 (COX-2) pathway is involved in the mitogenic pathway activated by Galpha12QL. Expression of Galpha12QL and not Galpha13QL, stimulates the serum-induced release of arachidonic acid in NIH3T3 cells. Furthermore, expression of Galpha12QL or the stimulation of wild-type Galpha12 induces the expression of COX-2. Our results also indicate that the COX-2 inhibitor acutely disrupts the DNA-synthesis stimulated by Galpha12QL in NIH3T3 cells. These studies, for the first time, identify the crucial role of COX-2 in Galpha12-mediated regulation of cell proliferation and suggest a role for prostaglandin-derived autocrine loop in Galpha12-mediated signaling pathways.

PMID: 10602471 [PubMed - indexed for MEDLINE]

1: J Rheumatol. 1998 Nov;25(11):2279-81. Related Articles, Links

Entrez PubMed

Comment on:
- J Rheumatol. 1997 Feb;24(2):243-5.
- J Rheumatol. 1997 Feb;24(2):246-8.

Roles of COX-1 and COX-2.

PubMed Services

McCormack K.

Publication Types:
- Comment
- Letter
- Review
- Review, Tutorial

PMID: 9818678 [PubMed - indexed for MEDLINE]

Related Resources

1: Inflamm Res. 1999 Mar;48(3):133-8.

Development of an in-vitro test system for the evaluation of cyclooxygenase-2 inhibitors.

Laufer S, Zechmeister P, Klein T.

Department Drug Research, Merckle GmbH, Blaubeuren, Germany.

OBJECTIVE AND DESIGN: The aim of our study was to establish an in-vitro test system, capable of fast and efficient screening of Cyclooxygenase-2 (COX-2) inhibitors. MATERIALS: Mononuclear cells were isolated out of human whole blood, in a one-step centrifugation procedure. TREATMENT AND METHODS: The time- and concentration-dependent induction of COX-2 expression in the blood monocytes (1 x 10(6) cells/ml) was evaluated by a kinetic profile. The optimal test conditions were fixed at an LPS concentration of 10 micrograms/ml and a 5 hour incubation time. The test compounds (10(-5) to 10(-8) mol/l) were set at t = 0 into the assay and were co-incubated for the whole period of COX-2 expression (5 hr). RESULTS: The following are representative examples of inhibitors with different distinct selectivity for COX-1/2. Indomethacin as a COX-1 selective compound inhibited PGHS-1 (IC50: 0.002 microM) 200 times stronger than PGHS-2 (IC50: 0.43 microM). Diclofenac had an almost equipotent efficacy on PGHS-1 (IC50: 0.05 microM) and PGHS-2 (IC50: 0.03 microM). NS-398 inhibited highly selective COX-2 (IC50 PGHS-1: 10.75 microM vs IC50 PGHS-2: 0.16 microM). CONCLUSIONS: The model reached the set targets with regard to the differentiation of COX-2 selective compounds, the reproducibility of results and practicability of the assay. In contrast to previous propounded theories, we could demonstrate, that mononuclear cells are not unusually sensitive to NSAIDs and apparently possess no further COX isoforms.

PMID: 10219655 [PubMed - indexed for MEDLINE]

NCBI PubMed National Library of Medicine NLM

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Books

Search PubMed for COX-2 AND arachidonic Go Clear

Limits Preview/Index History Clipboard Details

Field: **Title**

Display Summary Show: 20 Sort Send to Text

Items 1-2 of 2 One page.

Entrez PubMed

1: Rowlinson SW, Crews BC, Lanzo CA, Marnett LJ. Related Articles, Links

The binding of arachidonic acid in the cyclooxygenase active site of mouse prostaglandin endoperoxide synthase-2 (COX-2). A putative L-shaped binding conformation utilizing the top channel region.
J Biol Chem. 1999 Aug 13;274(33):23305-10.
PMID: 10438506 [PubMed - indexed for MEDLINE]

PubMed Services

2: Marnett LJ, Rowlinson SW, Goodwin DC, Kalgutkar AS, Lanzo CA. Related Articles, Links

Arachidonic acid oxygenation by COX-1 and COX-2. Mechanisms of catalysis and inhibition.
J Biol Chem. 1999 Aug 13;274(33):22903-6. Review. No abstract available.
PMID: 10438452 [PubMed - indexed for MEDLINE]

Related Resources

1: Biochem Soc Trans. 1990 Aug;18(4):503-7. Related Articles, Links

Entrez PubMed

Receptor-mediated activation of phospholipase A2 and arachidonic acid release in signal transduction.

Axelrod J.

PubMed Services

Laboratory of Cell Biology, National Institute of Mental Health, Bethesda, MD 20892.

Publication Types:
- Review
- Review, Tutorial

PMID: 2177403 [PubMed - indexed for MEDLINE]

Related Resources

Display Abstract Show: 20 Sort Send to Text

WEST

Generate Collection | Print

Search Results - Record(s) 1 through 12 of 12 returned.

☐ 1. Document ID: US 20030100591 A1

L6: Entry 1 of 12 File: PGPB May 29, 2003

PGPUB-DOCUMENT-NUMBER: 20030100591
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030100591 A1

TITLE: Methods of treatment of uterine pathological conditions

PUBLICATION-DATE: May 29, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Jabbour, Henry Nicolas	Edinburgh		GB	

US-CL-CURRENT: 514/383; 514/16, 514/17, 514/406, 514/423, 514/573, 514/605

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 2. Document ID: US 20030083465 A1

L6: Entry 2 of 12 File: PGPB May 1, 2003

PGPUB-DOCUMENT-NUMBER: 20030083465
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030083465 A1

TITLE: Therapeutic and diagnostic methods and compositions based on Jagged/Notch proteins and nucleic acids

PUBLICATION-DATE: May 1, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Zimrin, Ann B.	Marriottsville	MD	US	
MaCiag, Thomas	Freeport	ME	US	
Pepper, Michael S.	Geneve	PA	CH	
Montesano, Roberto	Geneve		CH	
Wong, Michael	Pittsburgh		US	

US-CL-CURRENT: 530/350; 435/320.1, 435/325, 435/69.1, 536/23.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 3. Document ID: US 20030022242 A1

L6: Entry 3 of 12 File: PGPB Jan 30, 2003

PGPUB-DOCUMENT-NUMBER: 20030022242
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030022242 A1

TITLE: Particles with improved solubilization capacity

PUBLICATION-DATE: January 30, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Anderson, David	Colonial Heights	VA	US	

US-CL-CURRENT: 435/7.1; 424/490

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments KWIC | Draw Desc | Image

---

☐ 4. Document ID: US 20020177551 A1

L6: Entry 4 of 12 File: PGPB Nov 28, 2002

PGPUB-DOCUMENT-NUMBER: 20020177551
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020177551 A1

TITLE: Compositions and methods for treatment of neoplastic disease

PUBLICATION-DATE: November 28, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Terman, David S.	Pebble Beach	CA	US	

US-CL-CURRENT: 514/12; 435/325, 530/350

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments KWIC | Draw Desc | Image

---

☐ 5. Document ID: US 20020177152 A1

L6: Entry 5 of 12 File: PGPB Nov 28, 2002

PGPUB-DOCUMENT-NUMBER: 20020177152
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020177152 A1

TITLE: COX 1-interacting proteins and use thereof

PUBLICATION-DATE: November 28, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Wettstein, Daniel Albert	Salt Lake City	UT	US	

US-CL-CURRENT: 435/6; 435/189, 435/320.1, 435/325, 435/69.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments KWIC | Draw Desc | Image

☐ 6. Document ID: US 20020022055 A1

L6: Entry 6 of 12 File: PGPB Feb 21, 2002

PGPUB-DOCUMENT-NUMBER: 20020022055
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020022055 A1

TITLE: Composition and methods for immproving integrity of compromised body passageways and cavities

PUBLICATION-DATE: February 21, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Signore, Pierre E	Vancouver British Columbia		CA	

US-CL-CURRENT: 424/486

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments KWIC | Draw Desc | Image

☐ 7. Document ID: US 6524795 B1

L6: Entry 7 of 12 File: USPT Feb 25, 2003

US-PAT-NO: 6524795
DOCUMENT-IDENTIFIER: US 6524795 B1

TITLE: Diagnostics for cardiovascular disorders

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments KWIC | Draw Desc | Image

☐ 8. Document ID: US 6451524 B1

L6: Entry 8 of 12 File: USPT Sep 17, 2002

US-PAT-NO: 6451524
DOCUMENT-IDENTIFIER: US 6451524 B1

TITLE: Identification of disease predictive nucleic acids

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments KWIC | Draw Desc | Image

☐ 9. Document ID: US 6433138 B1

L6: Entry 9 of 12 File: USPT Aug 13, 2002

US-PAT-NO: 6433138
DOCUMENT-IDENTIFIER: US 6433138 B1

TITLE: Therapeutic and diagnostic methods and compositions based on jagged/notch proteins and nucleic acids

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments KWIC | Draw Desc | Image

☐ 10. Document ID: US 6025194 A

L6: Entry 10 of 12 File: USPT Feb 15, 2000

US-PAT-NO: 6025194
DOCUMENT-IDENTIFIER: US 6025194 A

TITLE: Nucleic acid sequence of senescence asssociated gene

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments KWIC | Draw Desc | Image

☐ 11. Document ID: WO 200280927 A1 US 6440963 B1

L6: Entry 11 of 12 File: DWPI Oct 17, 2002

DERWENT-ACC-NO: 2002-697104
DERWENT-WEEK: 200278

TITLE: Method useful for treatment of neuromuscular dysfunction of lower urinary tract, e.g. dysuria, incontinence, enuresis and micturition disorders, involves use of selective inhibitors of cycloxygenase-2 isozyme

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments KWIC | Draw Desc | Clip Img | Image

☐ 12. Document ID: EP 1296971 A2 WO 200181332 A2 AU 200153749 A US 20020183362 A1

L6: Entry 12 of 12 File: DWPI Apr 2, 2003

DERWENT-ACC-NO: 2002-055338
DERWENT-WEEK: 200325

TITLE: New 2-fluorobenzenesulfonyl derivatives are cyclooxygenase2 inhibitors useful for treating inflammation, inflammation related disorders and cancer

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments KWIC | Draw Desc | Clip Img | Image

Generate Collection | Print

Terms	Documents
L1 same (G protein)	12

Display Format: - Change Format